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Diagnostic and Therapeutic Roles of Endoscopic Ultrasound in Pediatric Pancreaticobiliary Disorders

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ABSTRACT

Objectives: The diagnostic role of endoscopic ultrasound (EUS) in children has only recently been demonstrated, and that also to a lesser extent than in adults. Data on the technique's therapeutic indications remain scarce. We therefore sought to evaluate diagnostic and interventional EUS indications, safety, and impact in children with pancreaticobiliary disorders.

Methods: We retrospectively reviewed our single pediatric center records, covering a 14-year period.

Results: From January 2000 to January 2014, 52 EUS procedures were performed in 48 children (mean age: 12 years; range: 2–17 years) with pancreaticobiliary disorders for the following indications: suspected biliary obstruction (n = 20/52), acute/chronic pancreatitis (n = 20), pancreatic mass (n = 3), pancreatic trauma (n = 7), and ampullary adenoma (n = 2). EUS was found to have a positive impact in 51 of 52 procedures, enabling us to avoid endoscopic retrograde cholangiopancreatography (ERCP) (n = 13 biliary; n = 6 pancreatic), focusing instead on endotherapy (n = 7 biliary; n = 14 pancreatic) or reorienting therapy toward surgery (n = 7). EUS-guided fine-needle aspiration was carried out on 12 patients for pancreatic tumor (n = 4), pancreatic cyst fluid analysis (n = 4), autoimmune pancreatitis (n = 2), and suspicion of biliary tumor (n = 2). A total of 13 therapeutic EUS procedures (11 children) were conducted, including 9 combined EUS–ERCP procedures (7 children, mean age: 8 years, range: 4–11 years), 3 EUS-guided pseudocyst drainage (2 children), and 1 EUS-guided transgastric biliary drainage.

Conclusions: Our study reports on a large pediatric EUS series for diagnostic and therapeutic pancreaticobiliary disorders, demonstrating the impact of diagnostic EUS and affording insights into novel EUS and combined EUS–ERCP therapeutic applications. We suggest considering EUS as a diagnostic and therapeutic tool in the management of pediatric pancreaticobiliary diseases.

Key Words: autoimmune pancreatitis, biliary drainage, children, endoscopic ultrasonography, pancreatic cyst

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What Is Known

- Indications of endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) are rare in children.
- In adults, EUS has proven to be of particular interest in the diagnosis of obstructive jaundice.
- EUS-guided pancreatic cyst drainage is a less invasive therapeutic approach than surgery.

What Is New

- EUS and ERCP are complementary techniques for the diagnosis and treatment of pancreaticobiliary disorders that can be safely performed in children during the same session.
- Therapeutic EUS indications should be considered in children, including transluminal drainage of collections and biliary ducts.
- Contrast-enhanced EUS may help in the differential diagnosis of benign and malignant pancreat c masses.

Endoscopic ultrasound (EUS) is a well-established diagnostic tool for pancreaticobiliary diseases in adults. Since its development in the early 1980s, EUS has proven to be one of the most rapidly advancing fields in gastrointestinal (GI) endoscopy, opening up new endotherapy opportunities through its combination of endoscopic techniques and ultrasound (US) imaging.

EUS has been established as the most accurate diagnostic evaluation method for pancreatic cystic and mass lesions, pancreatic or biliary strictures, choledocholithiasis, and classifying pancreaticobiliary malignancy stages (1,2). Moreover, EUS enables a definitive diagnosis to be established on cytopathological/histopathological evaluation, using fine-needle aspiration (FNA) for the

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purposes of tissue and fluid analysis (3). Compared with conventional imaging, EUS displays a superior spatial resolution and more accurately detects structural pancreatic changes (4).

Therapeutic EUS indications can be divided into 2 main areas: EUS imaging as an aid to standard interventional endoscopic procedures and direct EUS-guided interventions, including drainage procedures and fine-needle injection therapies (2,5,6).

The combined use of endoscopic retrograde cholangiopancreatography (ERCP) and EUS procedures in the evaluation and treatment of pancreaticobiliary diseases has recently been described (7). This combined approach offers several advantages, including faster patient evaluation, enhanced efficiency, and avoiding repeated sedation.

In contrast with its regular use in adults, EUS is not commonly performed in children. This may be because of the limited number of pediatric indications, insufficient awareness among pediatricians and pediatric surgeons of the range of diagnostic and therapeutic indications, or the limited experience of pediatric endoscopists in performing EUS. Nonetheless, several authors have recently reported the use of EUS in the pediatric population, although their reports focused more on diagnosis (8–13) and less on single-step EUS-guided treatment (14,15). To the best of our knowledge, there has been next to no data provided on the role of a combined EUS–ERCP approach in the therapeutic management of pancreaticobiliary disease in children.

The present study sought to describe the indications of diagnostic and interventional EUS in pediatric pancreaticobiliary diseases and discuss the specific patients who benefited from a combined EUS–ERCP treatment.

METHODS

Patients

Between January 2000 and January 2014, all of the EUS procedures performed in children (<18 years old) admitted to our 150-pediatric-bed university hospital database were reviewed. Patients had been referred to our center by a pediatrician or pediatric surgeon. The demographic information, results of conventional abdominal imaging (US, computed tomography scan, magnetic resonance cholangiopancreatography, or magnetic resonance imaging), EUS indications, procedure details, outcome, and complications were all retrospectively analyzed. All of the EUS procedures were carried out by 3 experienced adult endoscopists (PD, IB, and TA). EUS was conducted for the following indications: negative or inconclusive results obtained using conventional imaging; diagnostic evaluation of pancreatic masses, suspected autoimmune pancreatic diseases, or ampullomas; drainage of pseudocysts when >5 cm or in the presence of symptoms or infection; and management of severe pancreatic pathologies by a combined EUS–ERCP approach.

The clinical impact of EUS was defined after clinical, biological, and radiological diagnostic workup and categorized into the following 4 grades:

0. No impact on diagnosis or management
1. Positive impact because of definitive diagnosis establishment
2. Positive therapeutic impact when EUS altered patient management strategy and ERCP-based endotherapy
3. Positive therapeutic impact with direct or combined EUS-guided treatment

Informed consent was obtained after discussing the procedures with the patients and their caregivers. The study protocol was approved by the institutional review board of the Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium.

Techniques

All of the procedures were performed in an interventional endoscopy suite, using fluoroscopic guidance if necessary, with an attending senior pediatric anesthesiologist. The children were examined under deep sedation or general anesthesia. Prophylactic antibiotics were administered only if the procedure had a therapeutic objective.

The procedures were carried out using linear echoendoscopes (FGUX-36, EG3830UT, Pentax, Hamburg, Germany, or GF-UCT180, Olympus, Aartselaar, Belgium) on a Hitachi 5500, 8500, or Aloka-SSD4000 processor (Hitachi, Hamburg, Germany). In children <3 years of age, a 20-MHz radial mini probe (Fuji, Düsseldorf, Germany) was inserted through the biopsy channel of an Olympus GIF-160 endoscope.

FNA was performed using either a 19-gauge or a 22-gauge FNA biopsy needle (EchoTip, ProCore, Wilson-Cook Medical Inc, Winston-Salem, NC). Color Doppler imaging was conducted to identify the vascular structures between the lesion and the GI tract. The puncture was made in an area that had no vessels in the needle tract, maintaining the smallest possible distance between the lesion and the GI lumen. To increase diagnostic accuracy, 2 to 4 needle passes were made.

Pancreatic pseudocyst drainage was performed in the following steps: 19-gauge needle puncture, opacification of the collection, insertion of a guidewire (Jagwire 0.035, Microvasive Endoscopy, Boston Scientific Corp, Galway, Ireland), cystogastrostomy or duodenostomy using a 5F, 8.5F, or 10F cystenterostome (Endoflex, Boucard, Belgium), and placement of a 7F or 10F double pigtail endoprosthesis (Endoflex) (16).

EUS-guided biliary drainage was carried out via bile duct puncture with a 19-gauge needle, followed by the placement of a guidewire threaded toward the hepatic hilum, dilation of the tract with an 8-mm balloon (MaxForce, Boston Scientific, Marlborough, MA), and placement of a 60-mm covered Wallstent (Boston Scientific), which was then deployed in the common bile duct (CBD) (16).

Contrast-enhanced harmonic endoscopic ultrasound (CEH-EUS) was used to differentiate pancreatic cancer from benign lesions. The echoendoscope was placed over the pancreatic area of interest. Bolus SonoVue (Bracco Imaging, Milan, Italy) was injected intravenously (dosage: 0.1 mL/year of age, maximum: 2 mL). Real-time continuous observation of the entire lesion was carried out progressively. The examination lasted for up to 150 seconds following injection for complete observation of the arterial and venous phases, with the initial 10 to 30 seconds considered the early phase, followed by the late phase (30–120 seconds).

Pathology

After FNA, the needle and syringe contents were rinsed in a vial containing a fixative according to the monolayer technique (Shandon Papspin, Thermo Fisher, Waltham, MA) (17,18). A maximum volume of 4 mL of the vial's contents was used to prepare 1 slide by cytocentrifugation so as to obtain a monolayer. All of the cytological slides were stained with Papanicolaou. The leftover material was fixed in 10% formalin, embedded in paraffin, cut into 5-μm-thick slides, and stained with hematoxylin and eosin. All of the slides were analyzed by an experienced cytopathologist (BW).

Statistical Analysis

The data were reported as median, range, and interquartile range (IQR) for continuous variables, and as relative frequencies for categorical variables. Fisher exact test was used to compare relative

frequencies. The unpaired Student *t* test with Welch correction was applied to compare populations because of unequal variance.

RESULTS

Patient Characteristics

Of the 11,000 EUS procedures conducted in our institution between January 2000 and January 2014, 52 (0.4%) were performed in children (n = 48) with pancreaticobiliary disease (19 boys and 29 girls; mean age: 12 years, range 2–17 years). All of the patients were monitored by a pediatric gastroenterologist. When a patient presented with a specific pancreaticobiliar pathology requiring EUS, the situation was discussed in a multidiscipline group, including the attending GI (echo) endoscopist. Pancreatic indications for EUS (30 EUS procedures in 26 children) were more frequent than biliary (22 EUS procedures) and observed in younger children (mean age: 10 years, range: 2 to 17 years and IQR 25%: 6 years for pancreatic indications, vs mean age: 15 years, range: 6 to 17 years, and IQR 25%: 13.5 years for biliary, $P < 0.0001$). Of these 52 EUS procedures, 45 (86%) were carried out under general anesthesia with endotracheal intubation.

The indications were as follows: suspected biliary obstruction based on clinical, biological, and radiological findings (n = 20/52); acute and chronic pancreatitis (n = 20); pancreatic trauma (n = 7); suspicious pancreatic mass (n = 3); and ampullary adenoma (n = 2). Depending on the EUS findings, ERCP was performed during the same general anesthesia, with biliary decompression in 5 patients, ampullectomy in 2 patients, and pancreatic sphincterotomy, drainage, or stenting in 14 patients. The indications for therapeutic EUS were pancreatic fluid collection or pseudocyst drainage (n = 12) and transluminal biliary drainage following failed ERCP cannulation (n = 1).

Details of the indications, EUS findings, and impacts have been presented in Table 1. The results of the conventional imagery findings, details on the children's characteristics, echoendoscopic material used, and patient follow-up times have been summarized in supplementary Table 1 (*http://links.lww.com/MPG/A421*). (Supplemental data in the submission file included a EUS decision tree figure, but no cross-reference included in text, so figure was not included.)

Common Bile Duct Obstruction

The most common indication for EUS procedure was suspected CBD obstruction (n = 20 children). On presentation, patients exhibited right upper abdominal quadrant pain, cholestasis, or suggestive transabdominal US (lithiasis or CBD dilatation), with 4 patients exhibiting associated increased lipase levels. In 13 patients, EUS was able to establish a diagnosis that precluded using ERCP.

In 4 patients, EUS revealed CBD stones and patients underwent stone extraction by ERCP. It should be emphasized that conventional US was unable to detect the biliary lithiasis in 1 of these patients.

In 1 patient, conventional imaging and EUS remained normal (Table 1, patient number 29). When performed at a later time, hepatobiliary iminodiacetic acid scan revealed a delayed bile clearance compatible with type II sphincter of Oddi dysfunction, according to the modified Milwaukee classification (19).

In another patient, a 13-year-old boy (Table 1, patient number 30), transabdominal US revealed intrahepatic bile duct dilatation and tapering of the CBD's distal portion. EUS detected reduced parenchymal echogenicity and a 22-mm hypoechogenic nodular lesion in the pancreatic head, with focal Wirsung duct narrowing and rim-like hypoattenuation. The elastographic pattern was green and considered benign, whereas CEH-EUS by intravenous SonoVue infusion revealed a perfusion of the lesion consistent with an inflammatory mass. EUS–FNA was performed and cytological/histological examination detected an inflammatory process with lymphoplasmacytic and polymorphonuclear cell infiltration. The proposed diagnosis was autoimmune pancreatitis (20). The patient underwent ERCP, during which biliary sphincterotomy, drainage, and stent placement were performed (Fig. 1).

Lastly, therapeutic EUS was performed in another 13-year-old boy with a metastatic rhabdomyosarcoma that obstructed the CBD and invaded the second part of the duodenum, rendering ERCP papilla cannulation impossible. EUS confirmed the presence of a 45-mm malignant mass in the pancreatic head and multiple metastatic lymph nodes. EUS-guided biliary drainage was carried out using a transgastric transcholedochal route, and a 60-mm covered metal stent was placed into the CBD. We opted for a covered stent of that specific length to avoid bile leakage between the stomach and CBD (Fig. 2; Table 1, patient number 31). On follow-up, jaundice resolved and liver enzymes normalized after 2 weeks.

Pancreatitis and Pancreatic Collections

EUS was performed in 18 children (20 procedures) with acute or chronic pancreatitis. Four patients (5 procedures) exhibited main pancreatic duct (MPD) stones, as revealed by EUS, and underwent ERCP for pancreatic sphincterotomy and stone extraction. A combined ERCP–EUS treatment approach was proposed for 2 children. One was found to have a pseudocyst (65×71 mm), which was drained by EUS-guided 10F double pigtail stent placement, and an endoprosthesis was placed into the MPD by ERCP. In the other child, EUS diagnosed pancreatic obstruction, intraductal stones, and a bleeding pseudocyst communicating with the MPD. For this patient, we performed sphincterotomy, stone extraction, MPD stenting, and EUS-guided placement of two 10F double pigtail stents in the pseudocyst, which achieved complete resolution of pain and bleeding (Table 1, patient number 6). Two years later, disease recurrence was observed and the patient successfully underwent the same EUS–ERCP procedure.

Three children met the endosonographic criteria for chronic pancreatitis without requiring further interventions, because they did not display intraductal stones, vascular pseudoaneurysm, or MPD anomalies.

Two children with suspected autoimmune pancreatitis, based on clinical and imaging findings, underwent diagnostic CEH-EUS and FNA. The elastographic pattern was green, and contrast harmonic imaging by intravenous SonoVue infusion revealed a perfusion of the lesion consistent with an inflammatory process. EUS–FNA was conducted. Cytopathological sample analysis detected lymphoplasmacytic and neutrophilic infiltrates that were compatible with the suspected diagnosis (20,21).

EUS was performed in 5 children, involving 6 procedures, for the purposes of either differential diagnosis or treatment of peri- or pancreatic fluid collections associated with acute or chronic pancreatitis. Of the 5, 2 patients were diagnosed as having a gastric duplication cyst and subsequently underwent successful surgical resection. In a third child (2 procedures) presenting with severe acute pancreatitis and exhibiting a large symptomatic pseudocyst (65×84 mm), transgastric drainage was carried out and a 7F and a 10F double pigtail stent were implanted. Two weeks later, acute arterial bleeding occurred around the drain site, which was managed by combined endoscopy–EUS techniques, along with adrenalin injection and the

TABLE 1. Patient characteristics, EUS findings, impact, and treatments

Patient	Age/sex	Indication	EUS findings	FNA	Impact	Treatment
Pancreatic patients						
1	5/F	Acute pancreatitis	Duplication cyst		2	Surgery
2	4/F	Acute pancreatitis	Pancreatic pseudocyst		3	EUS-guided pseudocyst drainage
3	13/F	Suspected autoimmune pancreatitis	Autoimmune pancreatitis	1	1	
4	2/M	Suspected autoimmune pancreatitis	Autoimmune pancreatitis	1	1	
5	11/M	Chronic pancreatitis	Pancreatic pseudocyst	1	3	EUS-guided pancreatic pseudocyst drainage
		Chronic pancreatitis; upper GI bleeding	Pseudocyst bleeding		3	EUS-guided pancreatic pseudocyst drainage
6	11/F	Chronic pancreatitis	Pancreatic pseudocyst (bleeding); MPD stones		3	EUS-guided pseudocyst drainage; ERP pancreatic sphincterotomy, stone extraction, MPD stenting
		Chronic pancreatitis	Pancreatic mass; MPD stones	1	2	ERP pancreatic sphincterotomy, stone extraction
7	17/M	Chronic pancreatitis	Chronic pancreatitis		2	ERP pancreatic sphincterotomy
8	17/F	Chronic pancreatitis	Chronic pancreatitis		1	
9	10/M	Chronic pancreatitis	Chronic pancreatitis + divisum		1	
10	16/F	Chronic pancreatitis	Chronic pancreatitis		1	
11	11/F	Chronic pancreatitis	Duplication cyst		2	Surgery
12	13/F	Chronic pancreatitis—GI malformation	Chronic pancreatitis		2	Surgery
13	17/M	Chronic pancreatitis	Chronic pancreatitis; MPD stones		2	ERP pancreatic sphincterotomy, stone extraction
14	16/F	Chronic pancreatitis	Chronic pancreatitis		2	ERP pancreatic sphincterotomy
15	5/F	Chronic pancreatitis	Pancreatic pseudocyst		3	EUS-guided pseudocyst drainage; ERP pancreatic sphincterotomy, MPD stenting
16	7/F	Chronic pancreatitis	Pancreatic pseudocyst MPD stones	1	3	EUS-guided pseudocyst drainage; ERP sphincterotomy, pancreatic stone extraction, MPD stenting
17	9/F	Chronic pancreatitis	Chronic pancreatitis; MPD stones		2	ERP sphincterotomy, pancreatic stone extraction
18	3/F	Chronic pancreatitis, upper GI bleeding, partial pancreatectomy	Chronic pancreatitis, no pseudoaneurysm		2	Surgery
19	2/F	Pancreatic mass, hyperinsulinism	Pancreatic mass	1	1	Surgery
20	16/F	Pancreatic mass	Pancreatic mass	1	2	Surgery
21	15/F	Pancreatic mass	Pancreatic mass	1	2	Surgery
22	10/F	Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst + fistula		3	EUS-guided pseudocyst drainage; ERP sphincterotomy, MPD stenting
23	11/M	Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst	1	3	EUS-guided pseudocyst drainage; ERP sphincterotomy, MPD stenting
		Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst		3	EUS-guided pseudocyst drainage; ERP MPD stenting
24	4/M	Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst		3	EUS-guided pseudocyst drainage; ERP sphincterotomy, MPD stenting
25	8/M	Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst		3	EUS-guided pseudocyst drainage; ERP sphincterotomy, MPD stenting
		Pancreatic trauma, acute fluid collection	Pancreatic pseudocyst	1	3	EUS-guided pseudocyst drainage; ERP sphincterotomy, MPD stenting
26	16/F	Pancreatic trauma, chronic pancreatitis	Chronic pancreatitis		1	
Biliary patients						
27	17/M	Ampullary adenoma	Ampulloma		0	Ampullectomy
28	13/M	Ampullary adenoma	Ampulloma		0	Ampullectomy
29	17/F	Cholestasis, abdominal pain/SOD?	Normal		0	
30	13/M	Cholestasis	Autoimmune pancreatitis/ choledochal stenosis	1	2	ERC sphincterotomy, bile duct dilatation, prosthesis placement
31	13/M	Cholestasis rhabdomyosarcoma	Malign biliary stricture	1	3	EUS-guided CBD drainage
32	16/M	Suspected choledocholithiasis	Normal		1	Preclude ERC

TABLE 1. (*Continued*)

Patient	Age/sex	Indication	EUS findings	FNA	Impact	Treatment
33	17/M	Suspected choledocholithiasis	Normal		1	Preclude ERC
34	17/M	Suspected choledocholithiasis	Choledocholithiasis		2	ERC sphincterotomy, stone extraction
35	17/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
36	17/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
37	17/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
38	16/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
39	6/M	Suspected choledocholithiasis	Normal		1	Preclude ERC
40	14/M	Suspected choledocolithiasis	Normal		1	Preclude ERC
41	17/M	Suspected choledocolithiasis	Normal		1	Preclude ERC
42	16/F	Suspected choledocolithiasis	Choledocholithiasis		2	ERC sphincterotomy, stone extraction
43	16/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
44	17/F	Suspected choledocholithiasis	Choledocholithiasis		2	ERC sphincterotomy, stone extraction
45	16/M	Suspected choledocholithiasis	Normal		1	Preclude ERC
46	15/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
47	17/F	Suspected choledocholithiasis	Normal		1	Preclude ERC
48	12/M	Suspected choledocholithiasis	Choledocholithiasis		2	ERC sphincterotomy, stone extraction

CBD = common bile duct; ERC = endoscopic retrograde cholangiography; ERP = endoscopic retrograde pancreatography; EUS = endoscopic ultrasonography; FNA = fine-needle aspiration; GI = gastrointestinal; MPD = main pancreatic duct; SOD = sphincter of Oddi dysfunction.

placement of 2 new cystogastrostomy 7F and 10F stents. Uneventful healing was observed and the stents migrated spontaneously after 6 months (Table 1, patient number 5).

Pancreatic Masses and Ampullomas

Of the 48 patients, 3 displayed suspicious pancreatic masses and 2 displayed ampullomas. A 2-year-old girl with congenital hyperinsulinism had a positive L-Dopa positron emission tomography scan for a focal lesion in the pancreatic head. Conventional imaging and EUS were, however, unable to detect any significant lesion or mass. The patient underwent, during the same anesthesia, surgical duodenopancreatectomy. Histopathological examination of the resected tissue revealed no abnormality (Table 1, patient number 19). When performed later on, genetic examination confirmed a diffuse form of the disease. Two girls ages 15 and 16 years exhibited cystic masses in the pancreatic head (72 and 81 mm, respectively). The imaging results indicated papillary cystic and solid tumors of the pancreas, and both diagnoses were confirmed by EUS–FNA, followed by successful surgical duodenopancreatectomy (Fig. 3; Table 1, patient number 20 and 21). Finally, during routine duodenal endoscopic follow-up, ampullomas were found in 2 children with familial adenomatous polyposis. EUS did not detect intraductal extension, and the children were successfully treated by ampullectomy.

Pancreatic Trauma

EUS was performed in 5 children (involving 7 procedures) following pancreatic blunt trauma. Pancreatic lesions were reported based on transabdominal US, computed tomography scan, or magnetic resonance imaging results and staged according to the American Association for the Surgery of Trauma classification (22). The first child experienced a grade II pancreatic trauma and subsequently developed chronic pancreatitis. EUS confirmed chronic pancreatitis, yet did not reveal any MPD lesions. Four other children presented grade III posttraumatic pancreatic injuries accompanied by complete pancreatic rupture at the corporeocaudal junction (patient number 22–24) or at the corporeocephalic junction (patient number 25). All of the children developed acute (peri) pancreatic fluid collections causing abdominal pain and vomiting. Pancreatic trauma was managed by combined EUS–ERCP procedures. Pancreatic sphincterotomy was performed with MPD stent placement. EUS-guided cystogastrostomy or cystenterostomy was carried out in the same session with the placement of a 7F and/or a 10F double pigtail stent. Two patients underwent repeat EUS-guided drainage because of inadequate resolution of fluid collection after the first session. Stents migrated spontaneously after 2 months, with complete resolution of the collections (Fig. 4; Table 1, patient number 22–25).

Issues Related to EUS Procedures

Two children developed hemorrhagic complications during the EUS procedure. The first (patient number 28) exhibited upper GI bleeding approximately 1 week (8 days) after an EUS diagnostic workup of an ampulloma and subsequent ampullectomy. His condition required endoscopic hemostatic treatment by application of a clip at the bleeding site. The second (patient number 5) exhibited acute arterial bleeding around the drain site 19 days after an EUS-guided pseudocyst drainage. The bleeding was managed by adrenalin injection and both cystogastrostomy stents were replaced. No technical issues were recorded.

DISCUSSION

The present study demonstrated EUS indications in children to be comparable to those described in adults, even if the pathology may differ between the 2 populations. All of the procedures were successfully completed, and the EUS findings significantly influenced both the diagnosis and the treatment of pediatric pancreaticobiliary disease. Combined EUS and ERCP approaches proved beneficial and should thus be considered when managing complex pediatric pancreatic or biliary diseases. The procedures were technically feasible and safe.

In line with previous studies (Table 2), our data confirmed that EUS played a significant role in establishing a definitive diagnosis and managing pediatric pancreatic or biliary disorders. Despite being established as an indispensable diagnostic and

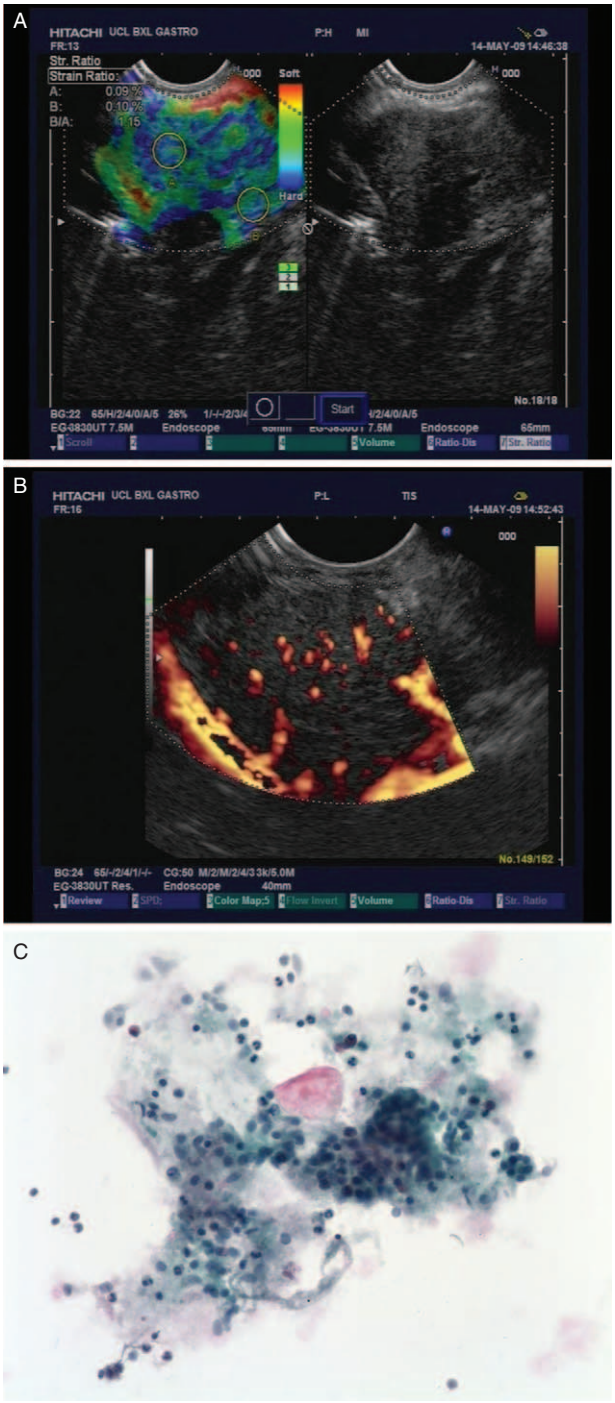

FIGURE 1. Autoimmune pancreatitis (patient number 30). (A) Endosonographic and elastographic views of the nodular lesion. The elastographic pattern is mainly green, suggesting an inflammatory process. (B) Contrast harmonic imaging by intravenous SonoVue infusion, demonstrating perfusion of the lesion consistent with an inflammatory mass. (C) A cytological picture of fine-needle aspiration showing a few ductal structures intermixed with chronic inflammatory cells and some eosinophils.

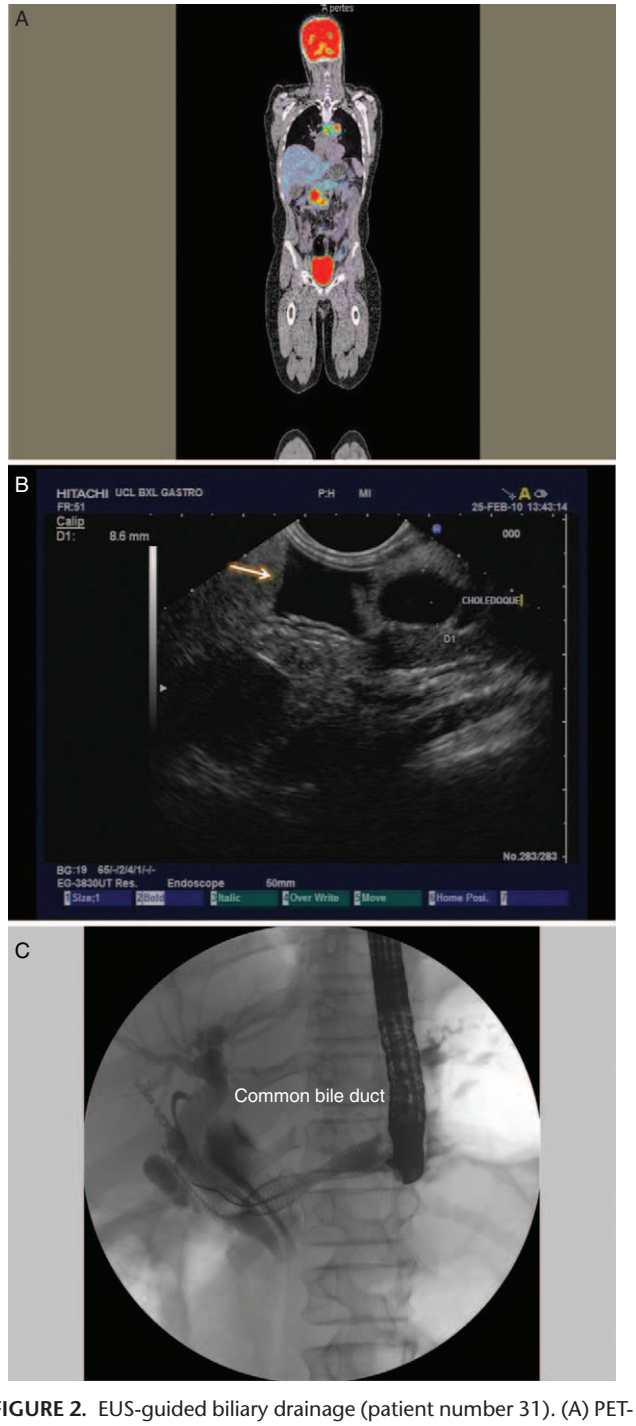

FIGURE 2. EUS-guided biliary drainage (patient number 31). (A) PET-CT showing a large pancreatic mass. (B) Endosonographic picture of a dilated CBD and presence of ascites (arrow). (C) Fluoroscopic imaging of the 2 covered metallic expandable stents placed in the CBD, with some surrounding leakage. CBD = common biliary duct; EUS = endoscopic ultrasound; PET-CT = positron emission tomography-computed tomography.

therapeutic modality in adult gastroenterology, EUS is rarely used in the pediatric population because of the limited patient numbers and poor levels of experience in performing the technique. Interestingly, our study proved that EUS conducted in children was a significant factor in avoiding ERCP, particularly in patients with clinical signs of CBD obstruction. In patients with pancreatic disease, EUS proved likely to alter patient management in favor of

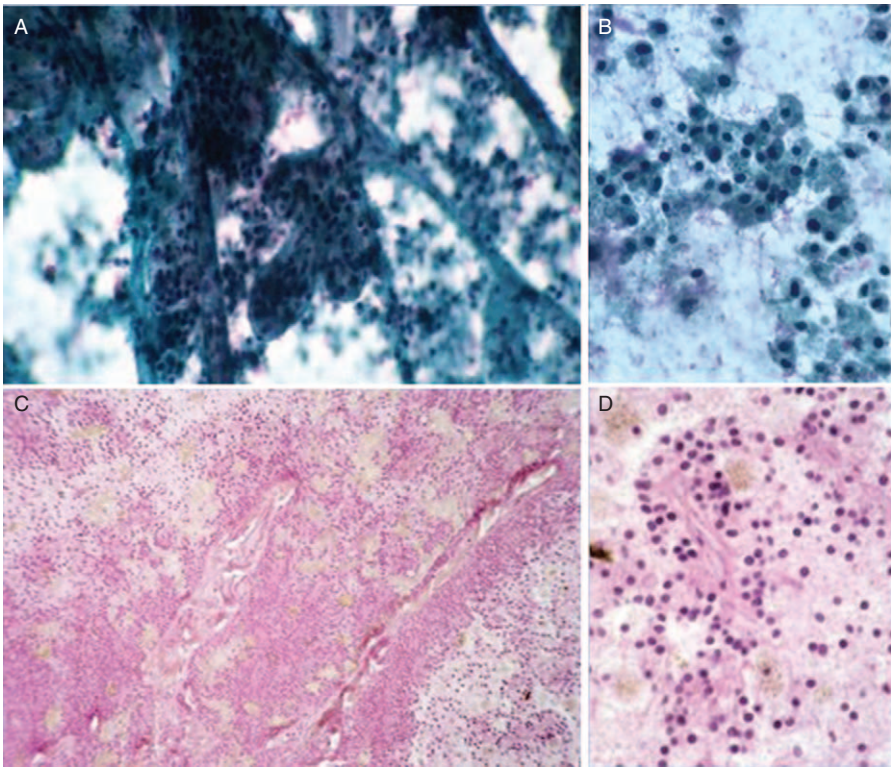

FIGURE 3. Solid pseudopapillary tumor of the pancreas (patient number 20). (A and B) Histopathology (Papanicolaou staining) of the pancreatic mass tissue obtained by fine-needle aspiration, demonstrating randomly arranged pseudopapillary structures. The fibrovascular axis is surrounded by poorly cohesive monomorphic epithelial cells at low (original magnification ×2.5—A) and high (original magnification ×20—B) magnification. (C and D) Histopathology (hematoxylin staining) of the surgical resection specimen, showing the same pseudopapillary architecture at (C) low and (D) high magnification.

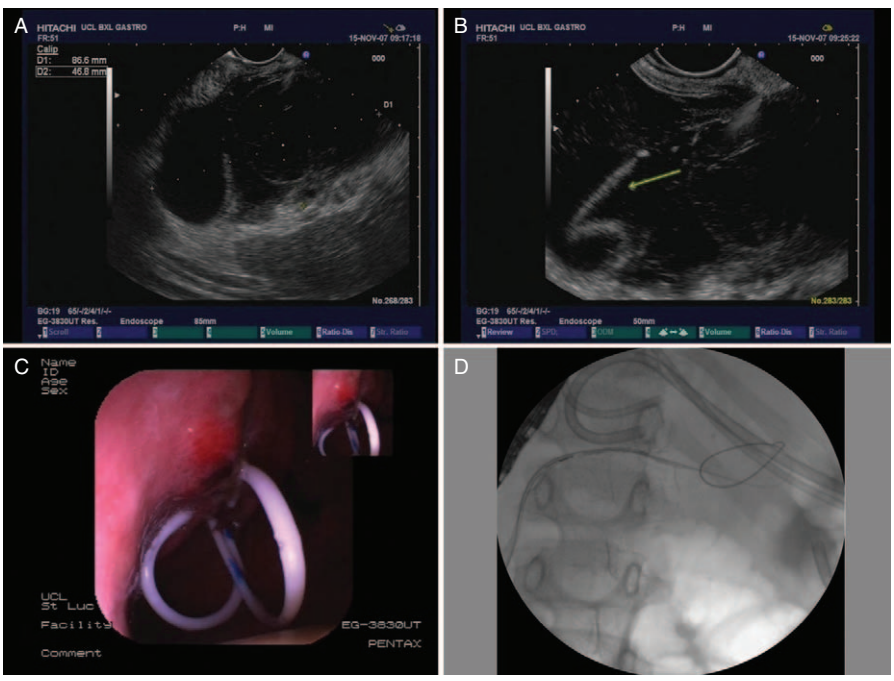

FIGURE 4. EUS-guided pancreatic pseudocyst drainage (patient number 22). (A) EUS imaging of the pseudocyst (arrow). (B) A 0.035-in. Jagwire inserted inside the cyst (arrow). (C) An endoscopic view of the 7F and 10F cystogastrostomy double pigtail plastic stents. (D) A fluoroscopic image of 2 cystogastrostomy plastic stents, with disruption of the pancreatic tail. The guidewire inserted into the MPD arrives via the fistula into the pseudocyst and coils inside the fluid collection. EUS = endoscopic ultrasonography; MPD = main pancreatic duct.

TABLE 2. Comparison of pediatric pancreaticobiliary EUS series

Study	Patients, total/PB	Impact	FNA, total/PB	Treatment, EUS/ERCP
Varadarajulu et al (9)	15/15	93%	3/3	0/5
Bjerring et al (10)	18/13	78%	1/1	0/1
Cohen et al (11)	32/19	44%	7/4	0/0
Attila et al (12)	38/25	NA	12/6	1/4
Al-Rashdan et al (13)	56/46	86%	15/12	5/5
Ramesh et al (14)	7/7	NA	NA	9/2
De Angelis et al (15)	13/13	NA	NA	4/0
Present study	52/52	98%	12/52	13/19

ERCP = endoscopic retrograde cholangiopancreatography; EUS = endoscopic ultrasonography; FNA = fine-needle aspiration; NA = not available; PB = pancreaticobiliary.

ERCP-based endotherapy or to exert a therapeutic effect when used as direct EUS-guided treatment ($P = 0.0006$).

In adults, EUS has been reported to be the most sensitive and highly specific diagnostic tool for choledocholithiasis and microlithiasis, while reducing the need for ERCP and its associated risks (23,24). In our series, of the 20 patients with suspected CBD obstruction after conventional imaging, 13 were concluded to be stone-free by EUS, thus avoiding undergoing ERCP. In 1 patient, EUS revealed CBD stones that were not seen with transabdominal US, allowing us to carry out biliary sphincterotomy and stone extraction via ERCP during the same session.

Reports on interventional diagnostic or therapeutic pancreaticobiliary EUS in the pediatric population are few and far between (14,15). The principal described indications have been EUS–FNA and pancreatic fluid collection drainage. In adults, EUS-guided pseudocyst drainage is the preferred management method of pancreatic fluid collections because of its high success rates, few complications, and decreased invasiveness (16,25,26). In the present study, 12 patients benefited from EUS-guided pseudocyst drainage. Only large (>5 cm diameter), symptomatic, or infected pseudocysts were drained. In our cohort, EUS was specifically used as the interventional diagnostic tool (EUS–FNA) in 5 of 52 procedures, all of them for pancreatic indications (autoimmune pancreatitis, n = 2; pancreatic mass, n = 4). EUS diagnosis relies on the echographic pattern of the lesions, elastography analysis of tissue hardness, contrast-enhanced imaging, and FNA. When combined, these tools may provide valuable information in challenging situations (27–30), such as atypical masses in chronic pancreatitis, cystic lesions, and pancreatic tumors or metastases. The exact role of this technique in the diagnosis of pediatric diseases has not yet been investigated. In this series, EUS pattern, elastography, and FNA carried out on 3 children with suspicious pancreatic masses were all indicative of an inflammatory mass, which was later corroborated by cytopathology as a sign of autoimmune pancreatitis. Despite the small sample size, our results were comparable to those obtained in adults in terms of success rate and diagnostic accuracy. We therefore suggest that the technique should also be applied to children. Finally, EUS-guided biliary drainage has proven efficient in adults for palliating malignant strictures in the event of cannulation failure or papilla that are inaccessible for ERCP (31–33). This technique has the advantage of being less invasive, decreasing morbidity, and enhancing the patient's quality of life compared with surgical or percutaneous drainage. We reported the first EUS-guided biliary drainage in a 13-year-old patient with metastatic rhabdomyosarcoma obstructing the biliary tract and involving the duodenum. During the same endoscopy session, the patient benefited from EUS-guided direct transgastric transcholedochal biliary drainage and the placement of a covered expandable metallic stent. The boy recovered quickly and his pain resolved within 24 hours.

Single endoscopic session treatments are gaining increasing acceptance in the adult population, and combined EUS and ERCP techniques have been demonstrated as safe and efficient for managing various pancreaticobiliary diseases during the same anesthesia in this population (7,34). We successfully combined EUS and ERCP during 22 of 52 procedures (42%), 14 for pancreatic indications and 8 for biliary. No complications were recorded. The benefits of the combined procedure include accelerating patient care and avoiding repeated sedations.

Based on the present data and the results of previously published works, we have proposed a list of diagnostic and therapeutic EUS indications for the management of pediatric pancreaticobiliary pathologies (Fig. 5).

Although the safety of diagnostic EUS has been well documented, therapeutic EUS may nevertheless be associated with complications, including bleeding, perforation, bile leakage, or infection (35). One of our patients presented a complication that was directly related to the EUS procedure. He developed gastric bleeding of the cystogastrostomy site 19 days after pancreatic fluid collection drainage. It should be noted that the patient was awaiting liver–kidney transplantation in the context of chronic hepatic and renal failure. A second child presented acute bleeding 8 days after undergoing an endoscopic resection of an ampulloma.

Adult echoendoscopes and accessories can be safely used in children >3 years of age (>15 kg body weight). In our series, 2 children were ≤3 years old, with the youngest being just 23 months. We found that the Pentax (FGUX-36, EG3830UT) or the Olympus (GF-UCT180) linear scopes were equally suitable for use in children. In children <3 years of age, mini probes were used. In children <6 years of age, the introduction of the echoendoscope should be performed with extra care to avoid GI perforation.

There were some limitations to the present study related to its retrospective nature. There was no standard protocol for imaging procedure before performing EUS, making it difficult to conclude on definitive recommendations. Comparison of best timing was not possible. Nevertheless, given the rarity of this pathology in the pediatric population, prospective studies appear particularly difficult to achieve in children. The age of the patients was unevenly distributed. A total of 25% of the patients, however, were ≤6 years of age, an age group for which the technique may pose the greatest challenge. Nevertheless, despite these limitations, the use of EUS for diagnostic and therapeutic interventions in children must now be considered.

In conclusion, we have reported on a large series of pediatric diagnostic and therapeutic EUS procedures for pancreaticobiliary indications. We demonstrated the significant role played by diagnostic EUS and high success rate of therapeutic EUS, both

Indication	Diagnostic/ therapeutic	References
Suspected choledocolothiasis/ microlithiasis*	D	(9,12,13,SD)
Suspected biliary strictures*	D	(20,SD)
Obstructive jaundice of unknown cause*	D/T— biliary drainage if papilla not accessible	(10,11,13,SD)
Cholangiocarcinoma/other tumors of CBD*	D-FNA/T— biliary drainage if papilla not accessible	SD
Ampulloma	D	(12,SD)
Pancreatic mass	D-FNA	(10–13,SD)
Suspected autoimmune pancreatitis	D-FNA	(12,21,SD)
Cystic pancreatic lesions	D/T — pseudocyst drainage when cyst>5 cm∅, symptomatic or infected	(10–15,SD)
Pancreatitis (acute, chronic, recurrent) from unknown origin	D	(9,10,12,13,21,SD)
Duplication cyst	D	(13,SD)
Coeliac plexus block	T	(12,13,SD)

FIGURE 5. Indications of diagnostic and therapeutic EUS procedures for pediatric pancreaticobiliary pathologies. *See also supplementary Figure 1. CBD = common bile duct; D = diagnostic; EUS = endoscopic ultrasonography; FNA = fine-needle aspiration; MPD = main pancreatic duct; SD = data related to the present study; T = therapeutic.

comparable to those reported in adults. We also considered novel pediatric indications, but performed them only on a small number of patients. Given that EUS is underused in children, we therefore suggest considering therapeutic EUS for pancreaticobiliary indications in children in a similar manner as that applied for adults.

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